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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HAMUD, FOZIA M	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 08/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/031,607	SAVITZKY ET AL.	
	Examiner	Art Unit	
	Fozia M Hamud	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26-53* is/are pending in the application.

4a) Of the above claim(s) *26, 27, 30-35, 37-53* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28,29 and 36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

Election/Restriction:

1a. Applicants' election filed on 06 February 2004 of the invention of Group II (claims 128-29, 36-37), drawn to an isolated polypeptide, without traverse is acknowledged.

Claim 37 was inadvertently placed in Group II. Claim 37 depends from claim 35, drawn to a pharmaceutical composition comprising an expression vector, which belonged to Group number I. Thus claim 37 is withdrawn.

1b. Applicants' election filed on 08 June 2004 of the polypeptide of SEQ ID NO:7, without traverse is also acknowledged.

Claims 28-29 and 36 will be searched and examined, in so far as they pertain to an isolated nucleic acid encoding the polypeptide of SEQ ID NO:7.

The restriction requirement is still deemed proper and is therefore made FINAL.

Claims 26-27, 30-35, 37 and 38-53 are withdrawn from consideration by the Examiner as they are drawn to non-elected inventions.

Information Disclosure Statement:

2a. All of the references cited on the PTO-1449 form submitted by Applicants on January/2002 have also been cited the PTO-1449 form submitted on June/2002. All of the submitted references have been considered, however, only one of the PTO-1449 forms has been initialed and signed.

Claim objections:

3a. Claims 28-29 and 36 are objected to because of the following informalities:

Claim 28 depends from a non-elected claim 26. Claim 29 is objected to because it recites non-elected SEQ ID Nos.

Claim 36 is objected to, insofar as it depends from claim 28. Appropriate correction is required.

Claim rejections-35 USC § 101:

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4a. Claims 26, 28-29 and 36 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility. Claim 26 is examined because elected claim 28 depends from it.

The claims of the instant invention are directed to an isolated polypeptide encoded by an isolated nucleic cid comprising a specific nucleotide sequence. The specification describes the nucleic acid of SEQ ID NO:1 as encoding a naturally occurring splice variant of human CD40 receptor, (see table I on page 4 and page 10, lines 8-11).

The instant specification discloses that the human CD40 splice variant of the instant invention comprises the extracellular domain of the native CD40 receptor. The specification asserts that the claimed CD40 receptor variant retains the ligand binding of the original CD40 receptor and thus is capable of binding to CD40 ligand (see page 10, lines 19-26).

However, while the instant specification asserts that the CD40 splice variant of the instant invention retains the ligand binding capabilities, it does not demonstrate that it actually binds to CD40 ligand. The native human CD40 receptor comprises 277 amino acid residues, while the instantly claimed CD40 receptor comprises 160 amino acid residues. The CD40 receptor claimed in the instant application shares only 135 amino acid residues with the native human CD40 receptor, and contains 25 amino acid residues that are not shared by the human CD40 receptor. The instant specification does not demonstrate that the claimed CD40 receptor retains the biological activities of the human CD40 receptor despite the differences that exist between them. Therefore, one of ordinary skill in the art would not know how to use the claimed polypeptide, because the instant specification does not establish the biological activity or significance of the claimed invention. The instant specification asserts that the variants of the invention are not merely truncated forms or fragments of the known gene, but rather novel sequences which naturally occur and which contain only the extracellular domain of the original CD40, (see page 10, lines 11-15), and thus bind to CD40 ligands. The specification further asserts that the CD40 receptor of the Instant invention can be used to treat diseases that can be ameliorated or cured by decreasing the levels of the CD40 ligands, (page 12, lines 17-20) and that it can be used to diagnose disorders that involve CD40 receptor, (page 10, lines 27-30). However, the instant specification does not demonstrate that the CD40 of the instant specification binds to CD40 ligands. Neither does it establish a connection between the claimed polypeptide and a specific

disease or disorder, but merely speculates that the claimed polypeptide are useful in treating and diagnosing diseases that involve CD40 receptor.

Thus, without showing that the CD40 receptor of the instant specification actually binds to CD40 lignds and without disclosing specific diseases/disorders that are treatable or diagnosable by the claimed polypeptide, a specific or substantial utility can not be established for said CD40 receptor or the nucleic acid encoding it.

4b. Claims 26, 28, 29 and 36 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a substantially asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. Applicants have not shown that the claimed CD40 receptor binds CD40 ligands. Neither has the specification shown which diseases or disorders can be treated or diagnosed using the polypeptide of the instant invention. Although the specification describes the structure of the polypeptide of SEQ ID NO:7 and discloses that it contains the extracellular domain of the native human CD40 receptor, it does not show that the claimed CD40 receptor actually binds to CD40 ligands nor have they shown that it treats or diagnoses a particular disease. Furthermore, the polypeptide of SEQ ID NO:7 only shares the first 135 amino acid residues of the native human CD40, and it comprises 25 amino acid residues that are not found in the native human CD40 receptor. However, Applicants have not shown that despite these differences the instant polypeptide still retains the activities of the native CD40 receptor. Therefore, there is no specific and substantial asserted utility or well established for the claimed polypeptide.

Even if Applicants establish an activity for the polypeptide of SEQ ID NO:2 encoded by the claimed nucleic acid, the instant specification would still fail to adequately enable a homologue of the polypeptide encoded by the nucleic acid of SEQ ID NO:6, wherein one or more amino acids have been added, deleted, replaced or chemically modified, or a polypeptide encoded by an isolated polypeptide encoded by a nucleic acid which is at least 90% identical to the nucleotide of SEQ ID NO:6. For example, Applicants do not teach which regions of the polypeptide of SEQ ID NO:7 can tolerate deletions, insertions or replacements of one amino acids or more, without affecting the activity of said polypeptide. Thus without information regarding which regions of the polypeptide of SEQ ID NO:7 are critical to a specific function, the full scope of the claimed invention is not enabled.

In summary, the amount of experimentation required for one of ordinary skill in the art to make and a homologue wherein one or more amino acids have been added, deleted, replaced or chemically modified, or a polypeptide encoded by an isolated nucleic acid which is at least 90% identical to the nucleotide of SEQ ID NO:6 would be undue. In Ex parte Forman, 230 USPQ 546 (Bd. Pat. Appls, and Interf. 1986), the Board considered the issue of enablement in molecular biology. The Board held that the following factors should be considered to determine whether the claimed invention would require of the skilled artisan undue experimentation: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or

unpredictability of the art and (8) the breadth of the claims. In the instant application, Applicants only disclose one polypeptide, said polypeptide comprising the amino acid sequence set forth in SEQ ID NO:7, and it will be undue experimentation to delineate "all" homologues, because Applicants have not taught which amino acid residues of SEQ ID NO:7 to alter without altering the desired activity. Furthermore, the state of the art is such that it is acknowledged that amino acid modifications of proteins is unpredictable, thus one of ordinary skill in the art would not be able to predict which amino acids to delete or to substitute while still preserving the desired activity. Neither has the specification disclosed where of the polypeptide of SEQ ID NO:7 to insert amino acids without altering the desired activity. There is no upper limit as to how many amino acids to replace, delete, or insert or which regions of the polypeptide are critical for its' function, the skilled artisan would not know how to make and use the claimed polypeptide.

The instant specification as filed also only describes the structure of the polypeptide of SEQ ID NO:7, and fails to describe "all" possible homologues of the polypeptide of SEQ ID NO:7. Therefore, conception is not achieved until reduction to practice has occurred. Adequate written description requires more than a mere statement that it is part of the invention.

To satisfy the written description requirement, an applicant's specification must reasonably convey to those skilled in the art that the applicant was in possession of the claimed invention as of the date of invention. Regents of the University of California v. Eli Lilly & Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1405 (Fed. Cir. 1997); Hyatt v.

Boone, 146 F.3d 1348, 1354, 47 USPQ2d 1128, 1132 (Fed. Cir. 1998). Furthermore, In The Reagents of the University of California v. Eli Lilly (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. Adequate written description requires more than a mere statement that it is part of the invention. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention". In the instant case, Applicants are claiming homologues of the polypeptide of SEQ ID NO:7, however, Applicants do not provide the structure of "all" possible homologues of the polypeptide of SEQ ID NO:7.

Therefore only the polypeptide comprising the amino acid sequence set forth in SEQ ID NO:7, but not the full breadth of the claims, meets the written description provision of 35 U.S.C. 112, first paragraph.

Claim Rejections - 35 U.S.C. § 112, second paragraph:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 28, 29 and 36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5a. Claim 28 recites "…. In which one or more amino acids have been added, deleted, replaced or chemically modified…", however it is unclear how many amino acids of the polypeptide of SEQ ID NO:7 to delete, insert or replace, how many to chemically modify and how. There is no upper limit for how many amino acids to alter, is it only one, ten or more? The metes and bounds of the claim cannot e ascertained.

Claims 29 and 36 are also rejected under 35 U.S.C. § 112, second paragraph, as being indefinite, so long as they depend from claim 28 for the limitations set forth directly above.

Claim Rejections - 35 U.S.C. §102:

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

6a. Claim 28 is rejected under U.S.C. § 102 (b) as being anticipated by Stamenkovic et al (1989), Accession Number A60771.

Stamenkovic et al disclose an isolated polypeptide that shares 86% over all homology to the polypeptide of SEQ ID NO:7 of the instant application. (See attached copies of the comparison of SEQ ID NO:7 of the instant invention and the sequence of the reference (SEQUENCE COMPARISON 'A').

Instant claim 28 is drawn to a homologue of the polypeptide of SEQ ID NO:7.

Therefore, the Stamenkovic et al reference anticipates the instant claim 28 in the absence of any evidence to the contrary.

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6b. Claims 28 and 36 are rejected under U.S.C. § 102 (b) as being anticipated by Aruffo et al (U.S Patent 6,376,459, effective filing date 31 August 1993).

Aruffo et al disclose human CD40 receptor and a pharmaceutical composition comprising said receptor and a suitable carrier, (see SEQ ID NO:2 and column 15, lines 37-46).

Instant claim 28 is drawn to a homologue of the polypeptide of SEQ ID NO:7 and claim 36 is drawn to a pharmaceutical composition comprising said homologue.

Therefore, the Aruffo et al reference anticipates the instant claims 28 and 36 in the absence of any evidence to the contrary.

Conclusion:

7. No claim is allowed.

Advisory Information:

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fozia M Hamud whose telephone number is (571) 272-0884. The examiner can normally be reached on Monday, Thursday-Friday, 6:00 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda G Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Fozia Hamud
Patent Examiner
Art Unit 1647
19 August 2004

JANET ANDRES
PRIMARY EXAMINER